PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*) 03 MAY 2005

Applicant's or agent's file reference
6395-68045

FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/08566	19 March 2004 (19.03.2004)	21 March 2003 (21.03.2003)

International Patent Classification (IPC) or both national classification and IPC
IPC(7): C 12 Q 1/06 and US Cl.: 702/23

Applicant
THE GOV. OF THE USA AS REP. BY THE SEC. HHS

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1. This opinion contains indications relating to the following items:

- [X] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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International application No.
PCT/US04/08566

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/08566

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 7, 12, 23	YES
	Claims 1-6, 8-11, 13-22, 24-30	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-30	NO
Industrial applicability (IA)	Claims 1-30	YES
	Claims NONE	NO

2. Citations and explanations:

1. Claims 1-6, 8-11, 13-22, and 24-30 lack novelty under PCT Article 33(2) as being anticipated by Wittwer et al. (US Patent 6,503,720 B2).

As to claims 1, 3, 5, 6, 8-10, 11, 13, 15, and 26-28, Wittwer et al. discloses for observation of a metric for a test sample, finding where on a usable portion of a standard sigmoid curve (Figs. 5 and 6) the observation lies, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve (Abstract, and col. 12, lines 14 and 15); and based on a location of the observation on the standard sigmoid curve, calculating a concentration of the substance (col. 12, lines 8-13. See also col. 9, line 66-col. 11, line 11 for a discussion of the relationship between serial dilutions and concentration determination) wherein the standard sigmoid curve represents a sigmoid curve fit to a plurality of optical density observations (col. 12, lines 10-13) taken of a reference sample having a known concentration of the substance (col. 12, lines 15-25).

As to claim 2, Wittwer et al. discloses that the sigmoid curve is represented via a four-parameter formula (col. 6, lines 4-10).

As to claims 4, 14, 17, 29, and 30, Wittwer et al. discloses determining whether the observation is above a threshold value (col. 8, lines 40-57), wherein the threshold value is determined via a first derivative of the standard sigmoid curve (col. 10, line 43- col. 11, line 2, as related to initial concentration determination. See also, col. 4, line 59-col. 5, line 8).

As to claim 16, Wittwer et al. discloses designating a portion between a minimum and a maximum of a second derivative for the sigmoid curve as the usable portion of the sigmoid curve (See Fig. 3A, MAX_1DER).

As to claims 18-22, 24, and 25, Wittwer et al. discloses that the features of the method of invention can be implemented using a concentration of live cells in a test sample, wherein the test sample is generated by adding test substances to cell cultures to study both inhibition and stimulation of the test substances (col. 11, line 65-col. 12, line 31. See also col. 5, lines 9-29).

2. Claims 7, 12, and 23, lack an inventive step under PCT Article 33(3) as being obvious over Wittwer et al. (US Patent 6,503,720 B2) in view of Kaastrup (United States Patent Application Publication US 2002/0160012 A1).

Wittwer et al. discloses the use of second-derivative sigmoid methods for determining a microbial stimulatory response as addressed above with respect to growth concentrations related to test samples A, B, and C.

Wittwer does not specifically disclose that the concentration indicates an amount of anti-PA IgG in the test sample.

Kaastrup, however, discloses that IgG is an important antibody in the human immune system that reacts with epitopes (or specific antigens) on invading microorganisms leading to the microorganisms' ultimate destruction (paragraphs 0007-0010). Kaastrup further notes that inclusion of an immunostimulating fragment is used to provide a protective immune response against anthrax (0236).

It therefore would have been obvious to extend the method taught by Wittwer et al. to the indication of amounts of anti-PA IgG in the test samples in order to provide continuous reliable determination of the presence and concentration of potentially lethal anthrax, as detected by sampling an individual's immune response.